PCT/EP99/04288
MediGene AG M26890PCUS BÖ/ps

PATENT CLAIMS

1. Structural protein of adeno-associated virus (AAV), which comprises at least one mutation, characterized in that the mutated structural protein is capable of particles formation, and the mutation brings about an increase in the infectivity of the virus.

2. Structural protein according to Claim 1, characterized in that the mutation(s) is/are located on the virus surface.

3. Structural protein according to claim 1, characterized in that the mutation(s) is/are located at the N terminus of the structural protein.

4. Structural protein according to claim 1, characterized in that the mutated structural protein brings about a change in the protein-cell membrane receptor interaction.

5. Structural protein according to Claim 4, characterized in that the cell membrane receptor is a glycoprotein of about 150 kD and/or a heparan sulphate proteoglycan.

6. Structural protein according to claim 1, characterized in that it is selected from mutated VP1, mutated VP2 and/or mutated VP3.

7. Structural protein according to claim 1, characterized in that it is derived from AAV2, AAV3, AAV4, AAV5 and/or AAV6.

8. Structural protein according to claim 1, characterized in that the mutation(s) is/are point mutation(s), mutation(s) of several amino acids, one or more deletions and/or one or more insertions, or a combination of this mutation.

9. Structural protein according to Claim 8, characterized in that the insertion is a cell membrane receptor ligand, a Rep protein or Rep peptide, an immunosuppressive protein or peptide and/or a protein or peptide having a signal for double-strand synthesis of the foreign gene.

10. Structural protein according to Claim 9, characterized in that the ligand is selected from an integrin, a cytokine or a receptor-binding domain of a cytokine, integrin or growth factor, a single-chain antibody binding to a cell surface receptor, an antibody against cell surface structures, an antibody-binding structure or an epitope, and from ligands which bind via their charge, the nature of the characteristic amino

acid composition and/or via their specific glycosilation and/or phosphorylation to cell surface molecules.

11. Structural protein according to claim 8, characterized in that the mutation(s) is/are brought about by one or insertions at the XhoI cleavage site of the VP1-encoding nucleic acid.

12. Structural protein according to claim 8, characterized in that the mutation(s) is/are brought about by one or insertions at the BsrBI cleavage site of the VP1-encoding nucleic acid.

13. Structural protein according to claim 8, characterized in that the mutation(s) is/are brought about by one or more deletions between the BsrBi/HindII cleavage sites of the VP1-encoding nucleic acid and one or more insertions.

14. Structural protein according to claim 8, characterized in that one or more insertions in VP3 is/are located before and/or after at least one amino acid in the sequence selected from YKQIS SQSGA, YLTLN NGSQA, YYLSR TNTPS, EEKFF PQSGV, NPVAT, EQYGS, LQRGN RQAAT, NVDFT VDTNG.

15. Structural protein according to Claim 8, characterized in that the mutation(s) is/are brought about by one or more deletions between

XhoI/XhoI cleavage sites of the VP1-encoding nucleic acid.

16. Structural protein according to Claim 8, characterized in that the mutation(s) is/are brought about by one or more deletions between BsrBI/HindII cleavage sites of the VP1-encoding nucleic acid.

17. Structural protein according to claim 1, in the form of an AAV particle, in particular in the form of an AAV capsid.

18. Nucleic acid coding for a structural protein according to claim 1.

19. Cell comprising a nucleic acid according to Claim 18.

20. Process for the preparation of a structural protein according to claim 1, characterized in that a cell according to Claim 19 is cultivated and, where appropriate, the expressed structural protein is isolated.

21. Medicinal product comprising a structural protein according to claim 1.

22. Medicinal product comprising a nucleic acid according to Claim 18.

23. Medicinal product comprising a cell according to Claim 19.

24. Diagnostic aid comprising a structural protein according to claim 1.

25. Diagnostic aid comprising a nucleic acid according to Claim 18.

26. Diagnostic aid comprising a cell according to Claim 19.

27. Method of using a structural protein according to claim 1 wherein the method is selected from the group consisting of altering the tropism of AAV, transforming a cell, diagnosis, activity investigations, gene therapy, and genomic targeting.

PATENT CLAIMS

1. Structural protein of adeno-associated virus (AAV), which comprises at least one mutation, characterized in that the mutated structural protein is capable of particles formation, and the mutation brings about an increase in the infectivity of the virus.

2. Structural protein according to Claim 1, characterized in that the mutation(s) is/are located on the virus surface.

3. Structural protein according to either of Claims 1 or 2, characterized in that the mutation(s) is/are located at the N terminus of the structural protein.

4. Structural protein according to any of Claims 1 to 3, characterized in that the mutated structural protein brings about a change in the protein-cell membrane receptor interaction.

5. Structural protein according to Claim 4, characterized in that the cell membrane receptor is a glycoprotein of about 150 kD and/or a heparan sulphate proteoglycan.

6. Structural protein according to any of Claims 1 to 5, characterized in that it is selected from mutated VP1, mutated VP2 and/or mutated VP3.

7. Structural protein according to any of Claims 1 to 6, characterized in that it is derived from AAV2, AAV3, AAV4, AAV5 and/or AAV6.

8. Structural protein according to any of Claims 1 to 7, characterized in that the mutation(s) is/are point mutation(s), mutation(s) of several amino acids, one or more deletions and/or one or more insertions, or a combination of this mutation.

9. Structural protein according to Claim 8, characterized in that the insertion is a cell membrane receptor ligand, a Rep protein or Rep peptide, an immunosuppressive protein or peptide and/or a protein or peptide having a signal for double-strand synthesis of the foreign gene.

10. Structural protein according to Claim 9, characterized in that the ligand is selected from an integrin, a cytokine or a receptor-binding domain of a cytokine, integrin or growth factor, a single-chain antibody binding to a cell surface receptor, an antibody against cell surface structures, an antibody-binding structure or an epitope, and from ligands which bind via their charge, the nature of the characteristic amino acid composition and/or via their specific glycosilation and/or phosphorylation to cell surface molecules.

11. Structural protein according to any of Claims 8 to 10, characterized in that the mutation(s) is/are brought about by one or insertions at the XhoI cleavage site of the VP1-encoding nucleic acid.

12. Structural protein according to any of Claims 8 to 10, characterized in that the mutation(s) is/are

brought about by one or insertions at the BsrBI cleavage site of the VP1-encoding nucleic acid.

13. Structural protein according to any of Claims 8 to 10, characterized in that the mutation(s) is/are brought about by one or more deletions between the BsrBi/HindII cleavage sites of the VP1-encoding nucleic acid and one or more insertions.

14. Structural protein according to any of Claims 8 to 10, characterized in that one or more insertions in VP3 is/are located before and/or after at least one amino acid in the sequence selected from YKQIS SQSGA, YLTLN NGSQA, YYLSR TNTPS, EEKFF PQSGV, NPVAT, EQYGS, LQRGN RQAAT, NVDFT VDTNG.

15. Structural protein according to Claim 8, characterized in that the mutation(s) is/are brought about by one or more deletions between XhoI/XhoI cleavage sites of the VP1-encoding nucleic acid.

16. Structural protein according to Claim 8, characterized in that the mutation(s) is/are brought about by one or more deletions between BsrBI/HindII cleavage sites of the VP1-encoding nucleic acid.

17. Structural protein according to any of Claims 1 to 16 in the form of an AAV particle, in particular in the form of an AAV capsid.

18. Nucleic acid coding for a structural protein according to any of Claims 1 to 16.

19. Cell comprising a nucleic acid according to Claim 18.

20. Process for the preparation of a structural protein according to any of Claims 1 to 16, characterized in that a cell according to Claim 19 is cultivated and, where appropriate, the expressed structural protein is isolated.

21. Medicinal product comprising a structural protein according to any of Claims 1 to 17, a nucleic acid according to Claim 18 and/or a cell according to Claim 19.

22. Diagnostic aid comprising a structural protein according to any of Claims 1 to 17, a nucleic acid according to Claim 18 and/or a cell according to Claim 19.

23. Use of a structural protein according to any of Claims 1 to 17 for altering the tropism of AAV, for transforming a cell, for diagnosis, for activity investigations, for gene therapy, and/or for genomic targeting.